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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/930,734	08/15/2001	Raymond F Horvath	98,313-C	3870

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EXAMINER
TRUONG, TAMTHOM NGO

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 09/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Notice of Non-Responsive Amendment

Applicant's amendment of 6-30-03 cannot be entered due to contradicting instructions. That is, claims 1-7, 12-19, 22-27, 29-50, and 52-67 are cancelled, and yet get amended. New claims 68-78 are not found. It is unclear as to which claims applicant intends to have.

The timely submission under 37 CFR 1.129(a) filed on 6-30-03 is not fully responsive to the prior Office action because it is not clear which claims are pending. Since the submission appears to be a *bona fide* attempt to provide a complete reply to the prior Office action, applicant is given a shortened statutory period of ONE MONTH or THIRTY DAYS from the mailing date of this letter, whichever is longer, to submit a complete reply. This shortened statutory period supersedes the time period set in the prior Office action. This time period may be extended pursuant to 37 CFR 1.136(a).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 703-305-4485. The examiner can normally be reached on M-F (5:00-12:30) & every Saturday morning (starting from 9-9-03).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 703-308-4716. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

T. Truong
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September 10, 2003

Alan L. Rotman

ALAN L. ROTMAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Parent A

FIRST ACTION ON MERIT

Priority

Applicant's claim of priority to a provisional application under 35 U.S.C. 119(e) is acknowledged.

Claim Rejections - 35 USC § 112

The following is a quotation of the **second paragraph** of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 6, 7, 18, 19, 23-27, 29, 30, 32, 33, 34, 43, and 51 recite the limitation, "R^8 is hydrogen", in their tricyclic compounds. There is insufficient antecedent basis for this limitation in said claims because hydrogen is not in the definition of R^8 as recited in claim 1. Note, claims 18, 19, 23-27, 29 30, 32, 33, 34, 43, and 51 do not recite the limitation, "R^8 is hydrogen", however, they recite species of "...-9H-pyrimidino[4,5-b]indole" which suggests R^8 as hydrogen.

Claims 31, 38, and 39 recite species of "...-5,6,7-trihydrocyclopenta[2,1-d]-8H-pyrimidino[4,5-b]indole" which suggest species of a tetracyclic system. There is insufficient antecedent basis for this limitation in said claims because, as recited in claim 1, R^2 and R^3 do not form a bicyclic system.

Claim 54 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See M.P.E.P § 2172.01. The omitted steps are those related to ring fusion, amination, alkylation, etc.

The following is a quotation of the **first paragraph** of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 31, 38, 39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. No preparation and use are provided for compounds of a tetracyclic system (i.e., 5,6,7-trihydrocyclopenta[2,1-d]-8H-pyrimidino[4,5-b]indole). Note, although the preparation of said species is referred to Example 1, one skilled in the art cannot obtain this complicated tetracylcic system without undue experimentation because the starting material in Example 1 is a substituted 4,5,6,7-tetrahydro-indole which ultimately get cyclized to become pyrimidino[4,5-b]indole (i.e., a tricyclic system). There is no suggestion on how one can obtain starting material for a tetracyclic system, or if such a starting material is commercially available. Thus, with the unpredictable nature of the art, undue experimentation is inevitable for one skilled in the art to make and use

said tetracyclic species. See, **In re Howarth, 210 USPQ 689; In re Lund, 153 USPQ 625; In re Fouche, 169 USPQ 429, regarding how to make and use.**

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7, 12-15, 17, 18, 22, 24, 27, 53-67 are rejected under 35 U.S.C. 102(a) as being anticipated by **Tanaka et. al.** (WO 98/29397 or WO'397). On pages 40 and 41, Tanaka et. al. disclose two formulae (43) and (44) that are embraced by the scope of the formula recited in claims 1-7, and 12-14, particularly when Ar represents a substituted phenyl group; R^2 and R^3 form a cyclohexyl or benzo group; and R^1 is an alkyl group. Furthermore, species in claims 15, 17, 18, 22, 24, and 27 are disclosed as compounds 46, 42, 47, 44, 51, and 45 (respectively) in ~~US~~ WO'397 (see pages 41, 113, 115-117, and 119). Claim 53 is a pharmaceutical composition which is apparently disclosed on page 46 because a dosage of 0.01 - 300 mg/person/day is stated on lines 7 and 8. Claim 54 is a process of making the claimed formula which is described on pages 39-41. Claims 55 and 56 are inherently embraced as it is well known in the art that any pharmaceutical

products would require at least a container and instruction. Claim 57 is a method for assaying the affinity of the claimed compounds for CRF receptor, and said method appears on page 121 of WO'397. Claims 58-60, and 64-67 are drawn to methods of inhibiting CRF receptors as well as treating related disorders which are disclosed throughout the document (see English abstract). Finally, compounds in claims 61-63 are embraced by the disclosed compounds as they have an IC_{50} of less than 500nM (see page 122, lines 1 and 2). Thus, at the time of the invention, one skilled in the art would have known how to make and use tricyclic compounds as claimed herein in view of Tanaka et. al.

Claims 1-4, and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by **Müller et. al.** (J. Med. Chem, 1990, Vol. 33 (10), pp. 2822-2828). In Table 1, Müller et. al. disclose compound #5 (type II and type III) which are embraced by the claimed formula, especially when R^1, R^4 and R^5 represent hydrogen while Ar represents a phenyl group di-substituted with C_1-C_6 alkoxy. Thus, at the time of the invention, one skilled in the art would have know how to make a tricyclic compound with such substituents in view of Müller et. al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7, 12-14, 16, 19, 22-27, 29, 30, 32-37, 40, 43-50, and 52-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tanaka et. al. Besides the species discussed in the 102(a) supra, Tanaka et. al. also provide two generic formulae (i.e., compounds 43 and 44) which allow for various permutations as their variables $R^{1'}$, R^2, R^3, R^8 - R^{10} represent more than one moiety. The scope of said formulae overlaps with that of the claimed formula recited in claims 1-7, 12-14, and embraces species in claims 16, 19, 22-27, 30, 32-37, 40, 43-50, and 52. Composition and method claims are taught by Tanaka et. al. as mention in the 102(a) supra. Thus, at the time of the invention, it would have been obvious to one of the ordinary skill in the art to make tricyclic compounds other than the ones anticipated by Tanaka et. al. (e.g., those with R^1 as hydrogen) because the generic teaching of Tanaka et. al. would have allow the skilled artisan to select said compounds and expect them to inhibit CRF receptors as well. Moreover, with respect to genus-species situations, the M.P.E.P. states that **"a generic chemical formula will *anticipate* a claimed species covered by the formula when the species can be *"at once envisaged"* from the formula."** (M.P.E.P. 2131.02) Such an issue of patentability has also been decided by the court in In re Susi, 440 F 2d. 442, 445, 169 USPQ 423, 425 (CCPA 1971), followed by the Federal Circuit in Merck & Co. v. Biocraft Laboratories, 874 F 2d. 804, 10 USPQ 2d. 1843, 1846 (Fed. Cir. 1989), and In re Swinehart, 169 USPQ 225, 229 (CCPA 1971).

Claim Objections

Claims 8-11, 20, 21, 28, and 51 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims, **excluding** overlapping subject matter disclosed by Tanaka et. al. and Müller et. al.

Regretfully, there is no translation of WO'397 at the present, applicants are requested to refer to the CAS print out for now. A corresponding US application of WO'397 has just been allowed, and will be published at a later time. It will be provided for applicants then.

A downloadable program is now available at this web site: **http://www.uspto.gov/printefs,** for applicants to print their own bibliographic information to avoid the need for corrected filing receipts.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mrs. Tamthom (or Tam) Truong whose telephone number is (703) 305 - 4485. The examiner can normally be reached on Monday thru Thursday from 7:30 am to 6:00 pm EST.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308 - 1235 or 305 - 3290.

T. Truong / 9-25-00

Mukund J. Shah

Mukund J. Shah
Supervisory Patent Examiner
Art Unit 1624